2/7/1 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

11764351 BIOSIS NO.: 199900010460
In conversion of solid into more anoxic ascites tumors associated with p53 inactivation?

AUTHOR: Magnusson Kristinn P(a); Satalino Rosa; Qian Wang; Klein George; Wiman Klas G
AUTHOR ADDRESS: (a)Microbiol. Tumor Biol. Cent., Karolinska Inst., Box 280, S-171 77 Stockholm, Sweden

JOURNAL: Oncogene 17 (18):p2333-2337 Nov. 5, 1998
ISSN: 0950-9232
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Most solid tumors are unable to grow in the ascites form, unless selected by prolonged serial transfer of peritoneal fluid (Klein, 1955). Established ascites tumor cells grow under highly crowded, virtually anoxic conditions (Warburg and Hiepler, 1953). Hypoxia was recently identified as a powerful inducer of p53 dependent apoptosis (Graeber et al., 1996). We wished to examine whether the conversion of relatively well-vascularized solid mouse tumors into freely growing ascitic cell variants favors cell with mutated or deleted p53. We have sequenced exons 4-9 of p53 cDNA from two serially transplanted methylcholanthrene induced sarcomas (MCIM and MSWBS) that were available in the original solid and the gradually converted ascites form. We have also examined five additional solid tumors, four carcinomas and one sarcoma and six additional ascites tumors, five carcinomas and one sarcoma. Sequence analysis showed that all solid tumors carried exclusively wild type p53. Among the eight ascites tumors, five carried mutant p53 and three bad only the wild type gene. In one of the two isogenic pairs, the original solid tumor line had only wild type, whereas the derived ascites tine had only mutant p53. In the second pair, the solid tumor was wild type whereas the ascitic variant was heterozygous. The naturally occurring alternatively spliced p53 (**p53as**) mRNA was detected in all solid tumors, but not in five of the eight ascites tumors. Our findings indicate that conversion of solid into ascites tumors favors the selection of cell variants with mutated p53 and of cells that lack the alternatively spliced form of p53.

2/7/2 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

11112088 BIOSIS NO.: 199799733233
Activities and response to DNA damage of latent and active sequence-specific DNA binding forms of mouse p53.

AUTHOR: Wu Yu; Huang Hua; Miner Zoe; Kulesz-Martin Molly(a)
AUTHOR ADDRESS: (a)Dep. Exp. Therapeutics, Roswell Park Cancer Inst., Elm Carlton Streets, Buffalo, NY 14263, USA

JOURNAL: Proceedings of the National Academy of Sciences of the United States of America 94 (17):p8982-8987 1997

ISSN: 0027-8424
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The mouse p53 protein generated by alternative splicing (**p53as**) has amino acid substitutions at its C terminus that result in constitutively active sequence-specific DNA binding (active form), whereas p53 protein itself binds inefficiently (latent form) unless activated by C-terminal modification. Exogenous **p53as** expression activated transcription of reporter plasmids containing p53 binding sequences and inhibited growth of mouse and human cells lacking functional endogenous p53. Inducible **p53as** in stably transfected p53 null fibroblasts increased p21-WAF1?-Cip-1/sdi and decreased bcl-2 protein steady-state levels. Endogenous **p53as** and p53 proteins differed in response to cellular DNA damage. p53 protein was induced transiently in normal keratinocytes and fibroblasts whereas **p53as** protein accumulation was sustained in parallel with induction of p21-WAF1/Cip-1/sdi and mRNA, in support of **p53as** transcriptional activity. Endogenous p53 and **p53as** proteins in epidermal tumor cells responded to DNA damage with different kinetics of nuclear accumulation and efficiencies of binding to a p53 consensus DNA sequence. A model is proposed in which C-terminally distinct p53 protein forms specialize in functions, with latent p53 forms primarily for rapid non-sequence-specific binding to sites of DNA damage and active p53 forms for sustained regulation of transcription and growth.

2/7/3 (Item 3 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

10896785 BIOSIS NO.: 199799517930
DNA binding specificity of proteins derived from alternatively spliced mouse p53 mRNAs.

AUTHOR: Miner Zoe; Kulesz-Martin Molly(a)
AUTHOR ADDRESS: (a)Roswell Park Cancer Inst., Dep. Exp. Therapeutics, GCDC Room 403 Carlton Streets, Buffalo, NY 14, USA

JOURNAL: Nucleic Acids Research 25 (7):p1319-1326 1997
ISSN: 0305-1048
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The mouse p53 gene generates two alternative splice products encoding p53 protein and a naturally occurring protein (**p53as**) with changes at the C-terminus. In **p53as** the negative regulatory region for DNA binding and PAb421 antibody binding site are replaced, and **p53as** is constitutively active for sequence-specific DNA binding. Using the technique of randomized synthetic oligonucleotide In cyclic amplification and selection of targets, we have found that **p53as** and p53 proteins have the same DNA binding specificities but that these specificities frequently diverge from the consensus of two copies of PuPuPuCATGPyPyPy. The importance of tetranucleotide CATG was confirmed but there was a less rigorous requirement for patterns of flanking or intervening sequences. In particular, the three purines upstream and three pyrimidines downstream of CATG are not required for p53 or **p53as** binding, 29 or more intervening nucleotides are tolerated, and one CATG is sufficient where adjacent nucleotides contain a region of homology with certain previously reported non-consensus p53 binding sequences. These results suggested further definition of the non-consensus motifs, and database searches with these uncovered additional candidate genes for p53 protein binding. We conclude that **p53as** and perhaps other activated forms of p53 exert their effects on the same genes and that differential activities of p53 protein forms

are not due to inherently different sequence selectivities of DNA binding.

2/7/4 (Item 4 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

10757792 BIOSIS NO.: 199799378937
The murine C'-terminally alternatively spliced form of p53 induces attenuated apoptosis in myeloid cells.

AUTHOR: Almog Nava; Li Runzhao; Peled Amnon; Schwartz Dov; Wolkowicz Roland ; Goldfinger Naomi; Pei Huiping; Rotter Varda(a)
AUTHOR ADDRESS: (a)Dep. Molecular Cell Biol., Weizmann Inst. Sci., Rehovot 76100, Israel

JOURNAL: Molecular and Cellular Biology 17 (2):p713-722 1997
ISSN: 0270-7306
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The onset of p53-dependent apoptosis results from the accumulation of damaged DNA. Recently, it was shown that the C' terminus of the p53 protein plays a central role in sensing damaged DNA. In our present study, we examined the role of the C' terminus in the induction of apoptosis. A temperature-sensitive (ts) mutant of the alternatively spliced form of p53 (**p53AS**-ts) and the ts mutant of the regularly spliced form (p53RS-ts) were used to generate series of stable clones with increasing amounts of p53 protein. Apoptotic patterns induced by either the regularly spliced p53 product (p53RS) or a C'-terminally alternatively spliced p53 product (**p53AS**) were compared. We found that although both forms of p53 induced apoptosis following expression of the wild-type protein conformation, the kinetics were different. Apoptosis induced by the **p53AS** protein was attenuated compared to that induced by p53RS. The delay in the manifestation of the apoptotic features following **p53AS** expression was in agreement with a delay in the regulation of the expression of apoptosis-related genes. The observation that p53 with an altered C' terminus is still capable of inducing apoptosis suggests that the actual onset of the apoptotic process most probably involves structural domains other than the C' terminus of the p53 molecule. However, the fact that the apoptotic activity mediated by the **p53AS** product was slower than that mediated by the p53RS product suggests that the C' terminus indeed exerts a certain control on the apoptotic activity of the p53 molecule.

2/7/5 (Item 5 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

10387120 BIOSIS NO.: 199699008265
Regulation of the cell cycle following DNA damage in normal and Ataxia telangiectasia cells.

AUTHOR: Lohrer H D
AUTHOR ADDRESS: Gray Lab., Mount Vernon Hosp., Northwood HA6 2JR, UK

JOURNAL: Experientia (Basel) 52 (4):p316-328 1996
ISSN: 0014-4754
DOCUMENT TYPE: Literature Review
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: A proportion of the population is exposed to acute doses of

ionizing radiation through medical treatment or occupational accidents, with little knowledge of the immediate effects. At the cellular level, ionizing radiation leads to the activation of a genetic program which enables the cell to increase its chances of survival and to minimize detrimental manifestations of radiation damage. Cytotoxic stress due to ionizing radiation causes genetic instability, alterations in the cell cycle, apoptosis, or necrosis. Alterations in the G1, S and G2 phases of the cell cycle coincide with improved survival and genome stability. The main cellular factors which are activated by DNA damage and interfere with the cell cycle controls are: p53, delaying the transition through the G1-S boundary; p21-WAFI/CIPI, preventing the entrance into S-phase; proliferating cell nuclear antigen (PCNA) and replication protein A (RPA), blocking DNA replication; and the p53 variant protein **p53as** together with the retinoblastoma protein (Rb), with less defined functions during the G2 phase of the cell cycle. By comparing a variety of radioresistant cell lines derived from radiosensitive ataxia telangiectasia cells with the parental cells, some essential mechanisms that allow cells to gain radioresistance have been identified. The results so far emphasise the importance of an adequate delay in the transition from G2 to M and the inhibition of DNA replication in the regulation of the cell cycle after exposure to ionizing radiation.

2/7/6 (Item 6 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

10359295 BIOSIS NO.: 199698814213
Differential induction of p53 and **p53as** DNA binding activities by DNA damage.

AUTHOR: Wu Y; Kulesz-Martin M
AUTHOR ADDRESS: Dep. Exp. Ther., Roswell Park Cancer Inst., Buffalo, NY 14263, USA

JOURNAL: Proceedings of the American Association for Cancer Research Annual Meeting 37 (0):p581 1996

CONFERENCE/MEETING: 87th Annual Meeting of the American Association for Cancer Research Washington, D.C., USA April 20-24, 1996
ISSN: 0197-016X
RECORD TYPE: Citation
LANGUAGE: English

2/7/7 (Item 7 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

09873067 BIOSIS NO.: 199598327985
The lytic replicon of bacteriophage P1 is controlled by an antisense RNA.

AUTHOR: Heinrich Jochen; Riedel Hans-Dieter; Rueckert Beate; Lurz Rudi; Schuster Heinz(a)
AUTHOR ADDRESS: (a)Max-Pianck Inst. Mol. Genetik, D-14195 Berlin, Germany

JOURNAL: Nucleic Acids Research 23 (9):p1468-1474 1995
ISSN: 0305-1048
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The lytic replicon of phage P1 is used for DNA replication during the lytic cycle. It comprises about 2% of the P1 genome and contains the P1 C1 repressor-controlled operator-promoter element Op53 cntdot P53 and

the kilA and the repL genes, in that order. Transcription of the lytic replicon of P53 and synthesis of the product of repL, but not kilA, are required for replicon function. We have identified an additional promoter, termed **P53as** (antisense), at the 5'-end of the kilA gene from which a 180 base transcript is constitutively synthesized and in the opposite direction to the P53 transcript. By using a promoter probe plasmid we show that transcription from P53 is strongly repressed by the C1 repressor, whereas that of **P53as** remains unaffected. Accordingly, the C1 repressor inhibits binding of Escherichia coli RNA polymerase to P53, but not to **P53as**, as shown by electron microscopy. Under non-repressed conditions transcription from P53 appears to be inhibited by **P53as** activity and vice versa. An inhibitory effect of **P53as** on the P1 lytic replicon was revealed by the construction and characterization of a **P53as** promoter-down mutant. Under non-repressed conditions transcription of repL and, as a consequence, replication of the plasmid is strongly enhanced when **P53as** is inactive. The results suggest a regulatory role for **P53as** on the P1 lytic replicon.

2/7/8 (Item 8 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

09582402 BIOSIS NO.: 199598037320
Wild-type alternatively splices p53: Binding to DNA and interaction with the major p53 protein in vitro and in cells.

AUTHOR: Wu Yu; Liu Yuangang; Lee Laura; Miner Zoe; Kulesz-Martin Molly(a)
AUTHOR ADDRESS: (a)Dep. Exp. Ther., Roswell Park Cancer Inst., Buffalo, NY 14263, USA

JOURNAL: EMBO (European Molecular Biology Organization) Journal 13 (20):p 4823-4830 1994
ISSN: 0261-4189
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: A p53 variant protein (**p53as**) generated from alternatively spliced p53 RNA is expressed in normal and malignant mouse cells and tissues, and **p53as** antigen activity is preferentially associated with the G-2 phase of the cell cycle, suggesting that **p53as** and p53 protein may have distinct properties. Using **p53as** and p53 proteins translated in vitro, we now provide evidence that **p53as** protein has efficient sequence-specific DNA-binding ability. DNA binding by p53 protein is inefficient in comparison and requires activation. Furthermore, **p53as** and p53 proteins formed hetero-oligomers when co-translated in vitro, resulting in inactivation of **p53as** DNA-binding activity. Gel filtration indicated that **p53as** translated in vitro, like p53, formed tetramers. In support of a functional role of **p53as** in cells, **p53as**/p53 hetero-oligomers were coimmunoprecipitated from mouse cells, and both protein forms were detectable in nuclear extracts by electrophoretic mobility shift assays. These results suggest that the biochemical functions of p53 are mediated by interaction between two endogenous protein products of the wild-type p53 gene.

2/7/9 (Item 9 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

09158408 BIOSIS NO.: 199497166778
Endogenous p53 protein generated from wild-type alternatively spliced p53

RNA in mouse epidermal cells.

AUTHOR: Kulesz-Martin Molly F(a); Lisafeld Barbara; Huang Hua; Kisiel Nicholas D; Lee Laura
AUTHOR ADDRESS: (a)Dep. Exp. Therapuetics, Roswell Park Cancer Inst., Buffallo, NY 14263, USA

JOURNAL: Molecular and Cellular Biology 14 (3):p1698-1708 1994
ISSN: 0270-7306
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: We previously demonstrated that a wild-type alternatively spliced p53 (**p53as**) RNA exists in mouse cultured cells and normal mouse tissues at approximately 25 to 33% of the level of the major p53 RNA form. The alternative RNA transcript is 96 nucleotides longer than the major transcript as a result of alternative splicing of intron 10 sequences. The protein expected to be generated from the **p53as** transcript is 9 amino acids shorter than the major p53 protein and has 17 different amino acids at the carboxyl terminus. We report here that **p53as** protein exists in nontransformed and malignant epidermal cells and is localized to the nucleus. In addition, **p53as** protein is preferentially expressed during the G-2 phase of the cell cycle and in cells with greater than G-2 DNA content compared with the major p53 protein, which is preferentially expressed in G-1. The **p53as** immunoreactivity is elevated and shifted to the G-1 phase of the cell cycle following actinomycin D treatment of nontransformed cells but not malignant cells. In view of the dimerization and tetramerization of p53 protein which may be necessary for its DNA binding and transcriptional activation activities, the presence of **p53as** protein in cells has important implications for understanding the physiological function(s) of the p53 gene.

2/7/10 (Item 1 from file: 73)
DIALOG(R)File 73:EMBASE

07460331 EMBASE No: 1998381798
Is conversion of solid into more anoxic ascites tumors associated with p53 inactivation?
Magnusson K.P.; Satalino R.; Qian W.; Klein G.; Wiman K.G.
K.P. Magnusson, Microbiology Tumor Biology Center, Karolinska Institute, Box 280, S-171 77 Stockholm Sweden
Oncogene (ONCOGENE) (United Kingdom) 05 NOV 1998, 17/18 (2333-2337)

CODEN: ONCNE ISSN: 0950-9232
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 25

Most solid tumors are unable to grow in the ascites form, unless selected by prolonged serial transfer of peritoneal fluid. Established ascites tumor cells grow under highly crowded, virtually anoxic conditions. Hypoxia was recently identified as a powerful inducer of p53 dependent apoptosis. We wished to examine whether the conversion of relatively well-vascularized solid mouse tumors into freely growing ascitic cell variants favors cell with mutated or deleted p53. We have sequenced exons 4-9 of p53 cDNA from two serially transplanted methylcholanthrene induced sarcomas (MCIM and MSWBS) that were available in the original solid and the gradually converted ascites form. We have also examined five additional solid tumors, four carcinomas and one sarcoma and six additional ascites tumors, five carcinomas and one sarcoma. Sequence analysis showed that all solid tumors carried exclusively wild type p53. Among the eight ascites tumors, five

carried mutant p53 and three had only the wild type gene. In one of the two isogenic pairs, the original solid tumor line had only wild type, whereas the derived ascites line had only mutant p53. In the second pair, the solid tumor was wild type whereas the ascitic variant was heterozygous. The naturally occurring alternatively spliced p53 (**p53as**) mRNA was detected in all solid tumors, but not in five of the eight ascites tumors. Our findings indicate that conversion of solid into ascites tumors favors the selection of cell variants with mutated p53 and of cells that lack the alternatively spliced form of p53.

2/7/11 (Item 1 from file: 159)
DIALOG(R)File 159:Cancerlit

01152565 96604453 ICDB/96604453
Antisense p53 inhibits apoptosis in myeloma cells through bcl-2 overexpression (Meeting abstract).
Iyer R; Ding L; Saylors R; Srivastava A; Barlogie B; Munshi N
Univ. of Arkansas for Medical Sciences, Little Rock, AR 72205
Proc Annu Meet Am Assoc Cancer Res; 36:A3337 1995 ISSN 0197-016X
Languages: ENGLISH
Document Type: MEETING ABSTRACTS
The P53 tumor suppressor gene is frequently mutated in a variety of human malignancies including multiple myeloma. On the basis of our initial observation that, at a very low concentration (10 nM), p53 antisense oligonucleotide stimulates proliferation of myeloma cells, we studied the effect of antisense p53 transduction in myeloma cells. Wild type p53 was introduced into ARH-77 myeloma cells using adeno-associated virus in an antisense (AS) or sense orientation under the control of herpes simplex TK promoter. P53 AS-transduced cells showed increased growth compared to controls as well as sense-p53 transduced cells. P53 mRNA and protein expression were decreased in the AS-transduced cells. Analysis of effects of p53-AS transduction revealed marked increase in bcl-2 expression without changes in c-myc or IL-6 expression. The increased expression of bcl-2 in p53-AS transduced cells was accompanied by a 10-fold decrease in apoptosis. Thus, the observed growth stimulation of ARH-77 cells upon **p53AS** transduction seems to be a reflection of decreased apoptotic cell death. Furthermore, we postulate that bcl-2 expression in myeloma may be regulated by p53 and its usual high levels may result from non-functional mutated p53.

2/7/12 (Item 2 from file: 159)
DIALOG(R)File 159:Cancerlit

01151400 96602422 ICDB/96602422
Transcriptional regulation by alternatively spliced p53 (Meeting abstract).
Huang H; Kulesz-Martin M
Roswell Park Cancer Institute, Buffalo, NY 14263
Proc Annu Meet Am Assoc Cancer Res; 36:A3419 1995 ISSN 0197-016X
Languages: ENGLISH
Document Type: MEETING ABSTRACTS
p53 acts as a transcription factor. A p53 variant protein (**p53as**) generated from alternatively spliced p53 RNA was found in our lab to be expressed in normal mouse cells and tissues and to bind p53-specific DNA sequences more efficiently than the major form of p53 (p53r). We hypothesize that **p53as** acts in transcriptional regulation differently from p53r. To test this hypothesis, several plasmids containing known p53-binding elements (the endogenous p53 target promoter WAF-1 or a synthetic p53 consensus sequence) upstream of a chloramphenicol acetyltransferase (CAT) or luciferase gene were co-transfected with **p53as** or p53r expression vectors into a p53-null mouse fibroblast

cell line and CAT or luciferase activity was assayed. CAT reporter plasmids without p53-binding sequences were assayed in parallel to evaluate transcriptional repression. Both **p53as** and p53r could activate transcription via the synthetic p53 consensus sequence and repress transcription from promoters without p53-binding sequences. The repressive effect of **p53as** was consistently about 2-fold stronger than that of p53r. However, in the case of the WAF-1 promoter, **p53as** acted as a transcriptional repressor at the same concentrations of transfected plasmid DNA at which p53r was an activator. These results suggest that p53 functions may be regulated by transcriptional activator and repressor proteins generated from the p53 gene by alternative splicing.

2/7/13 (Item 3 from file: 159)
DIALOG(R)File 159:Cancerlit

01147678 95608933 ICDB/95608933
Growth inhibition by expression of endogenous alternatively spliced p53 protein (Meeting abstract).
Wu Y; Kulesz-Martin M
Roswell Park Cancer Inst., Buffalo, NY 14263
Proc Annu Meet Am Assoc Cancer Res; 36:A1156 1995 ISSN 0197-016X
Languages: ENGLISH
Document Type: MEETING ABSTRACTS
Our laboratory has previously found a p53 variant protein (**p53as**) generated from alternatively spliced p53 mRNA in normal mouse cells and tissues. Cells which express **p53as** protein are preferentially distributed in the G2 phase of the cell cycle while cells expressing the major p53 protein are primarily in the G1 phase. Using proteins translated in vitro, we have shown that **p53as** protein has more efficient sequence-specific DNA-binding activity than p53 protein and does not require activation at the C terminus. **p53as** and p53 proteins form hetero-oligomers when cotranslated in vitro, resulting in inactivation of **p53as** DNA-binding activity. Moreover, **p53as** /p53 hetero-oligomers were detectable in mouse cells by co-immunoprecipitation as well as gel mobility shift assays. In order to directly examine the biological consequences of changes in the C terminus of **p53as** proteins, a **p53as** cDNA under the control of the metallothionein promoter was stably transfected into mouse fibroblasts lacking endogenous p53. Cells grew normally in the absence of the inducer, but induction of **p53as** expression by CdCl2 resulted in the dramatic inhibition of cell growth. Cell cycle dependence of this growth inhibition and the DNA binding activity of **p53as** in these cells are under evaluation. We hypothesize that the **p53as** protein plays a regulatory role in the control of cell growth by mechanisms distinct from p53.

2/7/14 (Item 4 from file: 159)
DIALOG(R)File 159:Cancerlit

01146711 95607966 ICDB/95607966
p53 control of cell cycle progression at G2/M (Meeting abstract).
Stewart NG; Hicks GG; Litchfield D; Mowat M
Manitoba Institute of Cell Biology, University of Manitoba, Winnipeg,, Manitoba, Canada R3E OV9
Proc Annu Meet Am Assoc Cancer Res; 36:A186 1995 ISSN 0197-016X
Languages: ENGLISH
Document Type: MEETING ABSTRACTS
Wild type p53 can induce cell cycle arrest at specific points of the cell cycle, such as transit through G1 and initiation of DNA synthesis. We recently demonstrated that p53 induces a second cell cycle block at G2/M. REF52 cell lines expressing the temperature sensitive p53val135 mutant allele were pulsed labeled with bromodeoxyuridine (S phase) before the

temperature shift. DNA flow cytometric analysis confirmed that a significant proportion of the S phase labelled cells arrested in G2/M (approx 30%) as well as G1 at the non-permissive temperature, but not in S phase. We are currently investigating the mechanisms behind this block. One possibility may involve the expression of the wild-type alternately spliced p53 variant **p53as** . This variant occurs at 25-33% the level of the major form and generates a protein 9 amino acid shorter and with 17 additional unique amino acids at the amino terminus. Interestingly, **p53as** is preferentially expressed at G2/M (compared to G1 for the major protein). Preliminary evidence suggests **p53as** is expressed in some of our cell lines. How **p53as** relates to our G2/M arrest point is currently under investigation. (2 Refs)

2/7/15 (Item 5 from file: 159)
DIALOG(R)File 159:Cancerlit

01068150 95605292 ICDB/95605292
Physiological protein variant of the mouse p53 tumor suppressor gene (Meeting abstract).
Wu Y; Kim SS; Kulesz-Martin M
Grace Cancer Drug Center and Dept. of Experimental Therapeutics, Roswell Park Cancer Inst., Buffalo, NY 14263
Proc Annu Meet Am Assoc Cancer Res; 35:A3607 1994 ISSN 0197-016X
Languages: ENGLISH
Document Type: MEETING ABSTRACTS
We have demonstrated previously that a wild-type alternatively spliced p53 (**p53as**) RNA exists in cultured cells and normal tissues [Han and Kulesz-Martin, Nucleic Acids Res 20:1979-81, 1992]. The protein expected to be encoded by the **p53as** transcript differs in 17 carboxyl terminal amino acids and is truncated by 9 amino acids due to alternative splicing of intron 10 of the p53 gene. Specific polyclonal antibody to a peptide unique to this **p53as** transcript was used to detect **p53as** protein in mouse epidermal cells. The **p53as** immunoreactivity was nuclear and was preferentially expressed during the G2 phase of the cell cycle and in cells with greater than G2 DNA content (based upon Hoechst DNA staining). In contrast, p53 immunoreactivity was preferentially expressed during G1 as expected from the literature. In order to determine whether **p53as** protein might functionally alter cell cycle-stage distribution, vectors containing full length **p53as** cDNA have been constructed and are being introduced into cells which lack p53 expression. Up to 12% of baculovirus-infected Sf9 insect cells expressed immunodetectable **p53as**. Of the **p53as** (+) cells, 2, 3, 15, and 80% had a DNA content indicative of G1, S, G2 and greater than G2, respectively, compared to 27, 25, 44, and 4% of control cells infected with vector only. These results suggest that the cells overexpressing **p53as** protein failed to progress to the G1/G0 phase of the cell cycle. We speculate that **p53as** may act at a cell cycle checkpoint distinct from the G1/S boundary patrolled by the major p53 protein form.

2/7/16 (Item 1 from file: 654)
DIALOG(R)File 654:US Pat.Full.

02788749
Utility
AMPLIFICATION OF HUMAN MDM2 GENE IN HUMAN TUMORS

PATENT NO.: 5,756,455
ISSUED: May 26, 1998 (19980526)
INVENTOR(s): Kinzler, Kenneth W., Baltimore, MD (Maryland), US (United States of America)
Vogelstein, Bert, Baltimore, MD (Maryland), US (United States

of America)
ASSIGNEE(s): The Johns Hopkins University, (A U.S. Company or Corporation), Baltimore, MD (Maryland), US (United States of America) [Assignee Code(s): 39884]
APPL. NO.: 8-390,515
FILED: February 17, 1995 (19950217)

This application is a divisional application of Ser. No. 08-044,619, filed Apr. 7, 1993, now U.S. Pat. No. 5,420,263, which is a continuation-in-part of Ser. No. 07-903,103, filed Jun. 23, 1992, now U.S. Pat. No. 5,411,860, which is a continuation-in-part of Ser. No. 07-867,840, filed Apr. 7, 1992, now abandoned.

FULL TEXT: 1692 lines

ABSTRACT

A human gene has been discovered which is genetically altered in human tumor cells. The genetic alteration is gene amplification and leads to a corresponding increase in gene products. Detecting that the gene, designated hMDM2, has become amplified or detecting increased expression of gene products is diagnostic of tumorigenesis. Human MDM2 protein binds to human p53 and allows the cell to escape from p53-regulated growth.
We claim:

1. A method for inhibiting the growth of tumor cells which contain a human MDM2 gene amplification, comprising:
administering to tumor cells which contain a human MDM2 gene amplification a DNA molecule which expresses a polypeptide consisting of a portion of p53, wherein said polypeptide comprises amino acids 1-50 of p53 as shown in SEQ ID NO:1, said polypeptide being capable of binding to human MDM2 as shown in SEQ ID NO:3.

2. A method for inhibiting the growth of tumor cells which contain a human MDM2 gene amplification, comprising:
administering to tumor cells which contain a human MDM2 gene amplification a DNA molecule which expresses a polypeptide consisting of a portion of p53, said portion comprising amino acids 13-41 of p53 as shown in SEQ ID NO:1 and at least nine additional p53 residues on either the amino or carboxy terminal side, wherein said polypeptide lacks the homo-oligomerization domain of p53, and said polypeptide is capable of binding to human MDM2 as shown in SEQ ID NO:3.

3. A method for inhibiting the growth of tumor cells which contain a human MDM2 gene amplification, comprising:
administering to tumor cells which contain a human MDM2 gene amplification a DNA molecule which expresses a polypeptide consisting of a portion of p53, said portion comprising amino acids 13-41 of p53 as shown in SEQ ID NO:1 and at least nine additional p53 residues on either the amino or carboxy terminal side, said polypeptide being capable of binding to human MDM2 as shown in SEQ ID NO:3, wherein said polypeptide lacks amino acids 138-393 of **p53as** shown in SEQ ID NO:6, 7, 8, or 9 and said polypeptide is capable of binding to human MDM2.

2/7/17 (Item 2 from file: 654)
DIALOG(R)File 654:US Pat.Full.

02779434
Utility
P53AS PROTEIN AND ANTIBODY THEREFOR

PATENT NO.: 5,747,650
ISSUED: May 05, 1998 (19980505)

INVENTOR(s): Kulesz-Martin, Molly F., Buffalo, NY (New York), US (United States of America)
ASSIGNEE(s): Health Research, Inc , (A U.S. Company or Corporation), Buffalo, NY (New York), US (United States of America) [Assignee Code(s): 11684]
APPL. NO.: 8-644,456
FILED: May 10, 1996 (19960510)

This is a continuation-in-part of U.S. patent application Ser. No. 08-106,496, filed Aug. 2, 1993.

This work was supported by a grant from the National Institutes of Health (CA 31101). The United States Government may have certain rights in the invention.

FULL TEXT: 1648 lines

ABSTRACT

In accordance with the present invention, we have discovered and purified a protein designated herein as **p53as** , which protein is present in normal cells of a mammal and is essentially identical to known normal growth controlling protein p53 of the same mammal, at least until the final 50 amino acids of the carboxy terminal end of the protein. The invention further includes an antibody specific for protein **p53as**, which antibody is designated herein as Ab **p53as**. The antibody may be either a monoclonal or polyclonal antibody and may be specific for **p53as** of any particular mammal such as mice and humans.
What is claimed is:

1. An antibody specific for a protein designated **p53as**, which protein is functionally equivalent with an active known normal growth controlling protein p53 of a mammal, the final amino acids of **p53as** protein proximate the carboxy terminus being sufficiently different than the carboxy terminus final 50 amino acids of the p53 protein, so that the **p53as** lacks a negative regulatory domain of said p53 and so that the **p53as** contains an epitope unique to **p53as** not present in said p53, said antibody being reactive with said epitope and not being reactive with said p53, said **p53as** functioning as a growth regulator in a manner similar to active p53 within cellular environments where said p53 loses activity due to loss of sequence specific binding by activation of said p53 negative regulatory domain.

2. The antibody of claim 1 wherein the **p53as** protein has an SPNC sequence in its carboxy terminal sequence (such SPNC sequence being shown in Seq. I.D. No. 1 as amino acids 14-17).

3. The antibody of claim 1 wherein the **p53as** protein has an SPPC sequence in its carboxy terminal sequence (such SPPC sequence being shown in Seq. I.D. No. 4 as amino acids 15-18).

4. The antibody of claim 1 wherein the antibody is a polyclonal antibody.

5. The antibody of claim 2 wherein the antibody is a polyclonal antibody.

6. The antibody of claim 3 wherein the antibody is a polyclonal antibody.

7. The antibody of claim 1 wherein the antibody is a monoclonal antibody.

8. The antibody of claim 2 wherein the antibody is a monoclonal antibody.

9. The antibody of claim 3 wherein the antibody is a monoclonal antibody.

10. The antibody of claim 1 wherein the **p53as** carboxy terminal

sequence is longer or shorter than the 50 amino acid terminal sequence of p53.

11. The antibody of claim 1 wherein the **p53as** is present in normal cells of the mammal.

2/7/18 (Item 3 from file: 654)
DIALOG(R)File 654:US Pat.Full.

02755955
Utility
P53AS PROTEIN AND ANTIBODY THEREFOR

PATENT NO.: 5,726,024
ISSUED: March 10, 1998 (19980310)
INVENTOR(s): Kulesz-Martin, Molly F., Buffalo, NY (New York), US (United States of America)
ASSIGNEE(s): Health Research, Inc , (A U.S. Company or Corporation), Buffalo, NY (New York), US (United States of America) [Assignee Code(s): 11684]
APPL. NO.: 8-644,291
FILED: May 10, 1996 (19960510)

This is a Continuation-in-part of U.S. patent application Ser. No. 08-259,612 filed Jun. 14, 1994 which is a Continuation-in-part of U.S. patent application Ser. No. 08-195,952 filed Feb. 11, 1994, now abandoned, which is a Continuation-in-part of U.S. application Ser. No. 08-100,496, filed Aug. 2, 1993.

This invention was made with support from National Cancer Institute Grant NIH RO1 CA 31101. The United States Government may have certain rights in the invention.

FULL TEXT: 1263 lines

ABSTRACT

The invention comprises plasmids and viral vectors containing an animal **p53as** cDNA sequence. A portion of the **p53as** sequence may be identified to a position of wild type p53 gene from the same animal. In preferred embodiments, the **p53as** is mouse or human **p53as**. A preferred viral vector is baculovirus vector. The invention further includes antibodies both polyclonal and monoclonal, to **p53as** and to at least a portion of human p53 intron 10 sequence encoding SLRPFKALVREKGHRPSSHSC (SEQ ID NO: 1) which is related to **p53as** sequences and plasmids and viral vectors containing such sequences. All of the above find utility in studying p53 and **p53as** and their relative expressions which is believed important for detection and control of malignant cells and their susceptibility to treatment agents. The antibodies can detect the presence of **p53as** and related sequences and when injected into cells could cause cell cycle arrest and the plasmids and viral vectors, with appropriate promotors, can cause expression of the **p53as** and p53 intron 10 sequences which can affect cell growth and perhaps arrest certain malignancies.
What is claimed is:

1. A method for determining the presence and concentration of **p53as** in a cell sample comprising:
a) reacting the cell sample with an antibody which specifically binds to mammalian **p53as** protein and does not bind to normal p53 from the same species wherein said antibody binds to an epitope present in a peptide unique to **p53as**, said peptide occurring within the final 50 carboxyl terminal amino acids of **p53as**;

b) determining the presence and concentration of **p53as** bound with said antibody; and
c) comparing the determined concentration of **p53as** in the cell sample with **p53as** concentrations in normal cell products.

2. The method of claim 1 wherein the normal p53 protein is a mouse p53 protein.

3. The method of claim 1 wherein the normal p53 protein is a human p53 protein.

4. The method of claim 1 wherein the antibody is a polyclonal antibody.

5. The method of claim 1 wherein the antibody is a monoclonal antibody.

2/7/19 (Item 4 from file: 654)
DIALOG(R)File 654:US Pat.Full.

02713890
Utility
P53AS PROTEIN AND ANTIBODY THEREFOR
[Antitumor]

PATENT NO.: 5,688,918
ISSUED: November 18, 1997 (19971118)
INVENTOR(s): Kulesz-Martin, Molly F., Buffalo, NY (New York), US (United States of America)
ASSIGNEE(s): Health Research, Inc , (A U.S. Company or Corporation), Buffalo, NY (New York), US (United States of America)
[Assignee Code(s): 11684]
APPL. NO.: 8-259,612
FILED: June 14, 1994 (19940614)

BACKGROUND OF THE INVENTION

This is a continuation-in-part of U.S. patent application Ser. No. 08-195,952 filed Feb. 14, 1994 which is a continuation in part of U.S. application Ser. No. 08-100,496, filed Aug. 2, 1993.

This invention was made with support from National Cancer Institute Grant NIH RO1 CA 31101. The United States Government may have certain rights in the invention.

FULL TEXT: 1257 lines

ABSTRACT

The invention comprises plasmids and viral vectors containing an animal **p53as** cDNA sequence. A portion of the **p53as** sequence may be identified to a position of wild type p53 gene from the same animal. In preferred embodiments, the **p53as** is mouse or human **p53as**. A preferred viral vector is baculovirus vector. The invention further includes antibodies both polyclonal and monoclonal, to **p53as** and to at least a portion of human p53 intron 10 sequence encoding SLRPFKALVREKGHRPSSHSC which is related to **p53as** sequences and plasmids and viral vectors containing such sequences. All of the above find utility in studying p53 and **p53as** and their relative expressions which is believed important for detection and control of malignant cells and their susceptibility to treatment agents. The antibodies can detect the presence of **p53as** and related sequences and when injected into cells could cause cell cycle arrest and the plasmids and viral vectors, with appropriate promotors, can cause expression of the **p53as** and p53 intron 10 sequences which can affect cell growth and perhaps arrest certain

malignancies.
What is claimed is:

1. An antibody which specifically binds to mammalian **p53as** protein and does not bind to normal p53 from the same species wherein said antibody binds to an epitope present in a peptide unique to **p53as**, said peptide occurring within the final 50 carboxyl terminal amino acids of **p53as**.

2. The antibody of claim 1 wherein the **p53as** protein is mouse **p53as** protein.

3. The antibody of claim 1 wherein the **p53as** protein is human **p53as** protein.

4. The antibody of claim 1 wherein the antibody is directed against at least a portion of human **p53as** protein having the sequence SLRPFKALVREKGHRPSHSC (SEQ ID NO.5) encoded by human **p53as** Intron 10 nucleic acid sequence.

5. The antibody of claim 4 wherein the antibody is a polyclonal antibody.

L1: 2 of 4

TITLE: **P53AS** protein and antibody therefor
US PAT NO: 5,747,650 DATE ISSUED: May 5, 1998
[IMAGE AVAILABLE]
APPL-NO: 08/644,456 DATE FILED: May 10, 1996
REL-US-DATA: Continuation-in-part of Ser. No. 100,496, Aug. 2, 1993.

L1: 3 of 4

TITLE: **p53as** protein and antibody therefor
US PAT NO: 5,726,024 DATE ISSUED: Mar. 10, 1998
[IMAGE AVAILABLE]
APPL-NO: 08/644,291 DATE FILED: May 10, 1996
REL-US-DATA: Continuation-in-part of Ser. No. 259,612, Jun. 14, 1994, which is a continuation-in-part of Ser. No. 195,952, Feb. 11, 1994, abandoned, which is a continuation-in-part of Ser. No. 100,496, Aug. 2, 1993.

L1: 4 of 4

TITLE: **p53as** protein and antibody therefor
US PAT NO: 5,688,918 DATE ISSUED: Nov. 18, 1997
[IMAGE AVAILABLE]
APPL-NO: 08/259,612 DATE FILED: Jun. 14, 1994
REL-US-DATA: Continuation-in-part of Ser. No. 195,952, Feb. 14, 1994, which is a continuation-in-part of Ser. No. 100,496, Aug. 2, 1993.

4/7/1 (Item 1 from file: 5)
DIALOG(R)File 5:BIOSIS PREVIEWS(R)

13378937 BIOSIS Number: 99378937
The murine C'-terminally *alternatively* *spliced* form of *p53* induces attenuated apoptosis in myeloid cells
Almog N; Li R; Peled A; Schwartz D; Wolkowicz R; Goldfinger N; Pei H; Rotter V
Dep. Molecular Cell Biol., Weizmann Inst. Sci., Rehovot 76100, Israel
Molecular and Cellular Biology 17 (2). 1997. 713-722.
Full Journal Title: Molecular and Cellular Biology
ISSN: 0270-7306
Language: ENGLISH
Print Number: Biological Abstracts Vol. 103 Iss. 005 Ref. 066815
The onset of p53-dependent apoptosis results from the accumulation of damaged DNA. Recently, it was shown that the C' terminus of the p53 protein plays a central role in sensing damaged DNA. In our present study, we examined the role of the C' terminus in the induction of apoptosis. A temperature-sensitive (ts) mutant of the *alternatively* *spliced* form of *p53* (p53AS-ts) and the ts mutant of the regularly *spliced* form (p53RS-ts) were used to generate series of stable clones with increasing amounts of p53 protein. Apoptotic patterns induced by either the regularly *spliced* *p53* product (p53RS) or a C'-terminally *alternatively* *spliced* *p53* product (p53AS) were compared. We found that although both forms of *p53* induced apoptosis following expression of the wild-type protein conformation, the kinetics were different. Apoptosis induced by the p53AS protein was attenuated compared to that induced by p53RS. The delay in the manifestation of the apoptotic features following p53AS expression was in agreement with a delay in the regulation of the expression of apoptosis-related genes. The observation that p53 with an altered C' terminus is still capable of inducing apoptosis suggests that the actual onset of the apoptotic process most probably involves structural domains other than the C' terminus of the p53 molecule. However, the fact that the apoptotic activity mediated by the p53AS product was slower than that mediated by the p53RS product suggests that the C' terminus indeed exerts a certain control on the apoptotic activity of the p53 molecule.

4/7/4 (Item 4 from file: 5)
DIALOG(R)File 5:BIOSIS PREVIEWS(R)

12127500 BIOSIS Number: 98727500
The human tumour suppressor gene *p53* is *alternatively* *spliced* in normal cells
Flaman J-M; Waridel F; Estreicher A; Vannier A; Limacher J-M; Gilbert D; Iggo R; Frebourg T
Lab. Genet. Mol., CHU Rouen, 76031 Rouen, France
Oncogene 12 (4). 1996. 813-818.
Full Journal Title: Oncogene
ISSN: 0950-9232
Language: ENGLISH
Print Number: Biological Abstracts Vol. 101 Iss. 008 Ref. 111775
Alternative splicing affecting the p53 carboxy-terminus has previously been described in mouse but not in normal human cells. We report here the detection in normal human lymphocytes of an *alternatively* *spliced* form of human *p53* mRNA containing an additional 133 hp exon derived from intron 9. This *splice* variant encodes a truncated protein of 341 amino-acids including 10 new amino-acids derived from the novel exon. The

truncated protein, which lacks part of the p53 tetramerization domain, fails to bind DNA in vitro and has a transcriptional defect in vivo in both yeast and mammalian cells. Quantitative RT-PCR experiments suggests that the alternatively spliced form is only present in significant amounts in quiescent cells. Considering the numerous functions ascribed to the carboxy-terminus of the p53 protein, this splice variant may have important implications for the biological role of p53 in normal cells.

4/7/5 (Item 5 from file: 5)
DIALOG(R)File 5:BIOSIS PREVIEWS(R)

√ Date

11962651 BIOSIS Number: 98562651
Species- and tissue-specific expression of the C-terminal *alternatively* *spliced* form of the tumor suppressor *p53*
Will K; Warnecke G; Bergmann S; Deppert W
Heinrich-Pette-Inst. Exp. Virol. Immunol., Univ. Hamburg, Martinistrasse 52, 20251 Hamburg, Germany
Nucleic Acids Research 23 (20). 1995. 4023-4028.
Full Journal Title: Nucleic Acids Research
ISSN: 0305-1048
Language: ENGLISH
Print Number: Biological Abstracts Vol. 101 Iss. 001 Ref. 005456
Alternative splicing of the p53 transcript which so far has been demonstrated only in the murine system has been proposed as a general regulatory mechanism for the generation of functionally different p53 proteins. We analyzed by RT-PCR the pattern of p53 mRNAs within the region spanning exons 10 and 11 of the p53 gene in 13 different tissues from two independent mouse strains, in 10 different rat tissues and in six different human tissues. PCR products of the expected sizes, corresponding to the normally *spliced* and the *alternatively* *spliced* *p53* mRNAs, were detected in mice. *Alternatively* *spliced* mRNA was found at apprx 25-30% the level of the normally *spliced* *p53* mRNA in most tissues analyzed. In spleen and kidney the only products of normal size. Although a potential homologous *alternative* 3' *splice* site within intron 10 of the human *p53* gene is present in the genomic sequence of human *p53*, the expected corresponding *alternatively* *spliced* *p53* mRNA was undetectable. These findings imply that the generation of functionally different forms of *p53* by *alternative* splicing of *p53* transcripts is a species-specific event, possibly indicating species-specific mechanisms for regulating p53 activities.

4/7/6 (Item 6 from file: 5)
DIALOG(R)File 5:BIOSIS PREVIEWS(R)

11915792 BIOSIS Number: 98515792
A splice donor site mutation results in the insertion of five extra amino acids into P53 from SEWA mouse sarcoma cells
Magnusson K P; Minarovits J; Klein G; Wiman K G
Microbiology Tumor Biology Cent., Karolinska Inst., Box 280, S-171 77 Stockholm, Sweden
Gene (Amsterdam) 162 (2). 1995. 231-234.
Full Journal Title: Gene (Amsterdam)
ISSN: 0378-1119
Language: ENGLISH
Print Number: Biological Abstracts Vol. 100 Iss. 011 Ref. 166649
The status of the p53 gene in SEWA-AS12-ADH (S-ADH) cells, a subline of the mouse sarcoma cell line SEWA, was examined. Immunoprecipitation with

wild-type (wt) or mutant P53-specific monoclonal antibodies (mAb) showed that both wt and mutant P53 were produced. Sequence analysis of the p53 cDNA and genomic DNA revealed a single nucleotide (nt) substitution at a *splice* donor site at the beginning of intron 7. As a result of this mutation, an *alternative* *splice* site 15 nt further 3' in intron 7 is used.. The *P53* protein translated from this aberrantly *spliced* mRNA carries an Arg-258 fwdarw Ser substitution, followed by an insertion of 5 extra amino acids. This is the first example of a splice-site mutation in the mouse p53 gene.

4/7/7 (Item 7 from file: 5)
DIALOG(R)File 5:BIOSIS PREVIEWS(R)

11822532 BIOSIS Number: 98422532
Augmented DNA-binding activity of *p53* protein encoded by a carboxyl-terminal *alternatively* *spliced* mRNA is blocked by *p53* protein encoded by the regularly *spliced* form
Wolkowicz R; Peled A; Elkind N B; Rotter V
Dep. Cell Biol., Weziman Inst. Sci., Rehovot 76100, Israel
Proceedings of the National Academy of Sciences of the United States of America 92 (15). 1995. 6842-6846.
Full Journal Title: Proceedings of the National Academy of Sciences of the United States of America
ISSN: 0027-8424
Language: ENGLISH
Print Number: Biological Abstracts Vol. 100 Iss. 007 Ref. 100124
DNA-binding activity of the wild-type p53 is central to its function in vivo. However, recombinant or in vitro translated wild-type p53 proteins, unless modified, are poor DNA binders. The fact that the in vitro produced protein gains DNA-binding activity upon modification at the C terminus raises the possibility that similar mechanisms may exist in the cell. Data presented here show that a C-terminal *alternatively* *spliced* wild-type *p53* (ASp53) mRNA expressed by bacteria or transcribed in vitro codes for a p53 protein that efficiently binds DNA. Our results support the conclusion that the augmented DNA binding activity of an ASp53 protein is probably due to attenuation of the negative effect residing at the C terminus of the wild-type p53 protein encoded by the regularly spliced mRNA (RSp53) rather than acquisition of additional functionality by the alternatively spliced C' terminus. In addition, we found that ASp53 forms a complex with the non-DNA-binding RSp53, which in turn blocks the DNA-binding activity of ASp53. Interaction between these two wild-type p53 proteins may underline a mechanism that controls the activity of the wild-type p53 protein in the cell.

4/7/8 (Item 8 from file: 5)
DIALOG(R)File 5:BIOSIS PREVIEWS(R)

11775471 BIOSIS Number: 98375471
The carboxyl-terminal domain of the p53 protein regulates sequence-specific DNA binding through its nonspecific nucleic acid-binding activity
Bayle J H; Elenbaas B; Levine A J
Dep. Mol. Biol., Lewis Thomas Lab., Princeton Univ., Princeton, NJ 08544, USA
Proceedings of the National Academy of Sciences of the United States of America 92 (12). 1995. 5729-5733.
Full Journal Title: Proceedings of the National Academy of Sciences of

the United States of America
ISSN: 0027-8424
Language: ENGLISH
Print Number: Biological Abstracts Vol. 100 Iss. 005 Ref. 067309
The murine p53 protein contains two nucleic acid-binding sites, a sequence-specific DNA-binding region localized between amino acid residues 102-290 and a nucleic acid-binding site without sequence specificity that has been localized to residues 364-390. *Alternative* splicing of mRNA generates two forms of this *p53* protein. The normal, or majority, *splice* form (NSp53) retains its carboxyl-terminal sequence-nonspecific nucleic acid-binding site, which can negatively regulate the sequence-specific DNA-binding site. The *alternative* *splice* form of *p53* (ASp53) replaces amino acid residues 364-390 with 17 different amino acids. This protein fails to bind nucleic acids nonspecifically and is constitutive for sequence-specific DNA binding. Thus, the binding of nucleic acids at the carboxyl terminus regulates sequence-specific DNA binding by p53. The implications of these findings for the activation of p53 transcriptional activity following DNA damage are discussed.

4/7/11 (Item 11 from file: 5)
DIALOG(R)File 5:BIOSIS PREVIEWS(R)

11601901 BIOSIS Number: 98201901
Transcriptional regulation by *alternatively* *spliced* *p53*
Huang H; Kulesz-Martin M
Roswell Park Cancer Inst., Buffalo, NY 14263, USA
Proceedings of the American Association for Cancer Research Annual Meeting 36 (0). 1995. 574.
Full Journal Title: Eighty-sixth Annual Meeting of the American Association for Cancer Research, Toronto, Ontario, Canada, March 18-22, 1995. Proceedings of the American Association for Cancer Research Annual Meeting
ISSN: 0197-016X
Language: ENGLISH
Print Number: Biological Abstracts/RRM Vol. 047 Iss. 005 Ref. 075564

4/7/12 (Item 12 from file: 5)
DIALOG(R)File 5:BIOSIS PREVIEWS(R)

11599642 BIOSIS Number: 98199642
Growth inhibition by expression of endogenous *alternatively* *spliced* *p53* protein
Wu Y; Kulesz-Martin M
Roswell Park Cancer Inst., Buffalo, NY 14263, USA
Proceedings of the American Association for Cancer Research Annual Meeting 36 (0). 1995. 194.
Full Journal Title: Eighty-sixth Annual Meeting of the American Association for Cancer Research, Toronto, Ontario, Canada, March 18-22, 1995. Proceedings of the American Association for Cancer Research Annual Meeting
ISSN: 0197-016X
Language: ENGLISH
Print Number: Biological Abstracts/RRM Vol. 047 Iss. 005 Ref. 073305

4/7/13 (Item 13 from file: 5)
DIALOG(R)File 5:BIOSIS PREVIEWS(R)

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11491981 BIOSIS Number: 98091981
Alternatively *spliced* forms in the carboxy-terminal domain of the *p53* protein regulate its ability to promote annealing of complementary single strands of nucleic acids
Wu L; Bayle J H; Elenbaas B; Pavletich N P; Levine A J
Dep. Mol. Biol., Princeton Univ., Princeton, NJ 08544-1014, USA
Molecular and Cellular Biology 15 (1). 1995. 497-504.
Full Journal Title: Molecular and Cellular Biology
ISSN: 0270-7306
Language: ENGLISH
Print Number: Biological Abstracts Vol. 099 Iss. 005 Ref. 062391
The carboxy-terminal domain of the p53 protein comprising amino acid residues 311 to 393 is able to promote the reassociation of single-stranded RNA or DNA into duplex hybrids. This domain is as efficient as the intact p53 protein in both the rate and the extent of the double-stranded product produced in this reaction. Both wild-type and mutant p53 proteins from cancerous cells carry out this reaction. The monoclonal antibody PAb421, which detects an epitope between residues 370 and 378, blocks the ability of *p53* to reassociate single strands of RNA or DNA. Similarly, the *alternative* *splice* form of the murine *p53* protein, which removes amino acid residues 364 to 390 and replaces them with 17 new amino acids, does not carry out the reassociation reaction with RNA or DNA. This is the first indication of functionally distinct properties of the *alternative* *splice* forms of *p53*. These results suggest that this *splice* *alternative* can regulate a *p53*-mediated reaction that may be related to the functions of this protein.

4/7/14 (Item 14 from file: 5)
DIALOG(R)File 5:BIOSIS PREVIEWS(R)
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11437320 BIOSIS Number: 98037320
Wild-type *alternatively* *splices* *p53*: Binding to DNA and interaction with the major *p53* protein in vitro and in cells
Wu Y; Liu Y; Lee L; Miner Z; Kulesz-Martin M
Dep. Exp. Ther., Roswell Park Cancer Inst., Buffalo, NY 14263, USA
EMBO (European Molecular Biology Organization) Journal 13 (20). 1994. 4823-4830.
Full Journal Title: EMBO (European Molecular Biology Organization) Journal
ISSN: 0261-4189
Language: ENGLISH
Print Number: Biological Abstracts Vol. 099 Iss. 002 Ref. 021864
A *p53* variant protein (p53as) generated from *alternatively* *spliced* *p53* RNA is expressed in normal and malignant mouse cells and tissues, and p53as antigen activity is preferentially associated with the G-2 phase of the cell cycle, suggesting that p53as and p53 protein may have distinct properties. Using p53as and p53 proteins translated in vitro, we now provide evidence that p53as protein has efficient sequence-specific DNA-binding ability. DNA binding by p53 protein is inefficient in comparison and requires activation. Furthermore, p53as and p53 proteins formed hetero-oligomers when co-translated in vitro, resulting in inactivation of p53as DNA-binding activity. Gel filtration indicated that p53as translated in vitro, like p53, formed tetramers. In support of a functional role of p53as in cells, p53as/p53 hetero-oligomers were coimmunoprecipitated from mouse cells, and both protein forms were detectable in nuclear extracts by electrophoretic mobility shift assays. These results suggest that the biochemical functions of p53 are mediated by

interaction between two endogenous protein products of the wild-type p53 gene.

4/7/15 (Item 15 from file: 5)
DIALOG(R)File 5:BIOSIS PREVIEWS(R)
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10966778 BIOSIS Number: 97166778
Endogenous *p53* protein generated from wild-type *alternatively* *spliced* *p53* RNA in mouse epidermal cells
Kulesz-Martin M F; Lisafeld B; Huang H; Kisiel N D; Lee L
Dep. Exp. Therapuetics, Roswell Park Cancer Inst., Buffallo, NY 14263, USA
Molecular and Cellular Biology 14 (3). 1994. 1698-1708.
Full Journal Title: Molecular and Cellular Biology
ISSN: 0270-7306
Language: ENGLISH
Print Number: Biological Abstracts Vol. 097 Iss. 008 Ref. 100448
We previously demonstrated that a wild-type *alternatively* *spliced* *p53* (p53as) RNA exists in mouse cultured cells and normal mouse tissues at approximately 25 to 33% of the level of the major p53 RNA form. The alternative RNA transcript is 96 nucleotides longer than the major transcript as a result of alternative splicing of intron 10 sequences. The protein expected to be generated from the p53as transcript is 9 amino acids shorter than the major p53 protein and has 17 different amino acids at the carboxyl terminus. We report here that p53as protein exists in nontransformed and malignant epidermal cells and is localized to the nucleus. In addition, p53as protein is preferentially expressed during the G-2 phase of the cell cycle and in cells with greater than G-2 DNA content compared with the major p53 protein, which is preferentially expressed in G-1. The p53as immunoreactivity is elevated and shifted to the G-1 phase of the cell cycle following actinomycin D treatment of nontransformed cells but not malignant cells. In view of the dimerization and tetramerization of p53 protein which may be necessary for its DNA binding and transcriptional activation activities, the presence of p53as protein in cells has important implications for understanding the physiological function(s) of the p53 gene.

4/7/16 (Item 16 from file: 5)
DIALOG(R)File 5:BIOSIS PREVIEWS(R)
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10108182 BIOSIS Number: 95108182
ALTERNATIVELY-*SPLICED* *P53* MRNA IN THE FAA-HTC1 RAT HEPATOMA CELL LINE WITHOUT THE *SPLICE* SITE MUTATIONS
FUKUDA I; OGAWA K
DEP. PATHOLOGY, ASAHIKAWA MED. COLL., 4-5-3-11 NISHIKAGURA, ASAHIKAWA, 078 JAPAN.
CELL STRUCT FUNCT 17 (6). 1992. 427-432. CODEN: CSFUD
Full Journal Title: Cell Structure and Function
Language: ENGLISH
A novel mutation of the p53 gene has been found in a rat hepatoma cell line, FAA-HTC1. This cell line carried two kinds of abnormal p53 transcripts; one lacked the exon 8 sequence, and the other had a single base substitution G to T which resulted in a new stop codon in exon 8. In the genomic DNA, this base substitution in exon 8 was present, indicating that both transcripts were transcribed from the mutated gene. No mutation was detected in its two flanking introns. In this cell line, the exon-deleted transcript seems to be generated by exon skipping due to an

unknown mechanism other than splice site mutations.

4/7/17 (Item 17 from file: 5)
DIALOG(R)File 5:BIOSIS PREVIEWS(R)

9525072 BIOSIS Number: 94030072
ALTERNATIVELY *SPLICED* *P53* RNA IN TRANSFORMED AND NORMAL CELLS OF DIFFERENT TISSUE TYPES
HAN K-A; KULESZ-MARTIN M F
DEP. EXPERIMENTAL THERAPEUTICS, GRACE CANCER DRUG CENTER, ROSWELL PARK CANCER INSTITUTE, BUFFALO, N.Y. 14263, USA.
NUCLEIC ACIDS RES 20 (8). 1992. 1979-1981. CODEN: NARHA
Full Journal Title: Nucleic Acids Research
Language: ENGLISH
The *alternatively* *spliced* RNA species of tumor suppressor gene *p53*, containing an additional 96 bases derived from intron 10, is present at approximately 25 to 30% the level of regularly *spliced* *p53* RNA in both normal epidermal and carcinoma cells. The presence of this *alternatively* *spliced* RNA in 10T1/2 fibroblast cells, mouse liver and testis suggests that this alterantive splicing may be universal. The level of *alternatively* *spliced* *p53* RNA was increased coordinately with that of regularly *spliced* *p53* in 10T1/2 cells in response to epidermal growth factor. Immunoprecipitation analysis of epidermal cells using monoclonal antibodies which recognize different epitopes of p53 suggested that distinct p53 proteins may be translated from both RNA species. Considering previous observations on the potential importance of carboxyl terminal sequences in *p53* function, knowledge of the ubiquitous presence of *alternatively* *spliced* *p53* is important for future studies of *p53* function in normal cells and in oncogenesis.

4/7/19 (Item 1 from file: 159)
DIALOG(R)File 159:Cancerlit

01266867 96633988 ICDB/96633988
The carboxyl-terminal domain of p53 is involved in transcriptional regulation (Meeting abstract).
Li PZ; Peled A; Elkind B; Rotter V
Dept. Molecular Cell Biology, The Weizmann Inst. of Science, Rehovot 76100, Israel
Proc Annu Meet Am Assoc Cancer Res; 37:A3988 1996 ISSN 0197-016X
Languages: ENGLISH
Document Type: MEETING ABSTRACT
It has been suggested that the sequence-specific DNA-binding activity of p53, which is central to its transcriptional regulation properties, is regulated by the C'-terminal domain of the protein. In order to examine the possibility that the C'-terminal domain is involved in the regulation of transcription, temperature sensitive, regular *spliced* (*p53*-RSts) and *alternative* *spliced* (*p53*-ASts) *p53* proteins were expressed in M1/2 cells. Using reverse transcriptase polymerase chain reaction, we examined the expression of p53 responsive genes at permissive temperature. Expression of both the p53-RSts and p53-ASts proteins activated expression of cyclin G and WAF1 upon the temperature shift from 37 C to 32 C. However, down-regulation of Bcl-2 and Myc and up-regulation of MDM2 were found in cells expressing p53-RSts while the level of mRNA expression of these genes in cells expressing p53-ASts was unchanged. In addition, p53-RSts increased the level of the GADD45 transcript while p53-ASts transrepressed this gene. These results suggest that the C'-terminal domain of p53 protein may be

involved in the transcription regulation of specific p53-responsive genes.

4/7/20 (Item 2 from file: 159)
DIALOG(R)File 159:Cancerlit

01256527 96633985 ICDB/96633985
Differential induction of p53 and p53as DNA binding activities by DNA damage (Meeting abstract).
Wu Y; Kulesz-Martin M
Dept. Experimental Therapeutics, Roswell Park Cancer Inst., Buffalo, NY 14263
Proc Annu Meet Am Assoc Cancer Res; 37:A3985 1996 ISSN 0197-016X
Languages: ENGLISH
Document Type: MEETING ABSTRACT
p53as protein, a *p53* gene product generated from the *alternatively* *spliced* *p53* transcript is expressed in mouse tissues and cultured normal and tumor cells. This protein has 17 different and 9 fewer amino acids than p53 protein and these structural changes result in altered biochemical function. p53as binds to p53 consensus sequences efficiently, while p53 protein binds specifically but inefficiently unless activated by modifications at the C terminus. Inducible expression of exogenous p53as in p53-null mouse cells resulted in the inhibition of cell growth and flow cytometry indicated that cells were arrested at multiple points in the cell cycle. Our previous finding that cells expressing endogenous p53as were differentially distributed in the G2 phase of the cell cycle relative to p53 suggested differences in biological function. This notion was supported by distinct kinetics of induction of p53as and p53 following DNA damage, as detectable by indirect immunostaining, immunoblotting of protein, and sequence-specific DNA binding activities. The induction of p53 antigen activity and protein was rapid and transitory, peaking within 3 hours. Induction of p53as antigen activity and protein, in comparison, was sustained after an initial lag phase. The transitory induction of p53 antigen activity and protein was coincident with a rapid induction of the latent DNA binding form of p53. The increase in p53as protein was accompanied by an induction of p53as homo- and p53as/p53 hetero-oligomers which were active in sequence-specific DNA binding. These findings imply distinct roles for active and latent DNA binding forms of p53 protein in cells responding to DNA damage.

4/7/22 (Item 4 from file: 159)
DIALOG(R)File 159:Cancerlit

01070808 95605292 ICDB/95605292
Physiological protein variant of the mouse p53 tumor suppressor gene (Meeting abstract).
Wu Y; Kim SS; Kulesz-Martin M
Grace Cancer Drug Center and Dept. of Experimental Therapeutics, Roswell Park Cancer Inst., Buffalo, NY 14263
Proc Annu Meet Am Assoc Cancer Res; 35:A3607 1994 ISSN 0197-016X
Languages: ENGLISH
Document Type: MEETING ABSTRACT
We have demonstrated previously that a wild-type *alternatively* *spliced* *p53* (p53as) RNA exists in cultured cells and normal tissues [Han and Kulesz-Martin, Nucleic Acids Res 20:1979-81, 1992]. The protein expected to be encoded by the p53as transcript differs in 17 carboxyl terminal amino acids and is truncated by 9 amino acids due to alternative splicing of intron 10 of the p53 gene. Specific polyclonal antibody to a

peptide unique to this p53as transcript was used to detect p53as protein in mouse epidermal cells. The p53as immunoreactivity was nuclear and was preferentially expressed during the G2 phase of the cell cycle and in cells with greater than G2 DNA content (based upon Hoechst DNA staining). In contrast, p53 immunoreactivity was preferentially expressed during G1 as expected from the literature. In order to determine whether p53as protein might functionally alter cell cycle-stage distribution, vectors containing full length p53as cDNA have been constructed and are being introduced into cells which lack p53 expression. Up to 12% of baculovirus-infected Sf9 insect cells expressed immunodetectable p53as. Of the p53as(+) cells, 2, 3, 15, and 80% had a DNA content indicative of G1, S, G2 and greater than G2, respectively, compared to 27, 25, 44, and 4% of control cells infected with vector only. These results suggest that the cells overexpressing p53as protein failed to progress to the G1/G0 phase of the cell cycle. We speculate that p53as may act at a cell cycle checkpoint distinct from the G1/S boundary patrolled by the major p53 protein form.

4/7/26 (Item 1 from file: 434)
DIALOG(R)File 434:Scisearch(R) Cited Ref Sci

14315169 Genuine Article#: TD372 Number of References: 44
Title: SPECIES-SPECIFIC AND TISSUE-SPECIFIC EXPRESSION OF THE C-TERMINAL *ALTERNATIVELY* *SPLICED* FORM OF THE TUMOR-SUPPRESSOR *P53*
Author(s): WILL K; WARNECKE G; BERGMAN S; DEPPERT W
Corporate Source: UNIV HAMBURG,HEINRICH PETTE INST EXPTL VIROL & IMMUNOL,MARTINISTR 52/D-20251 HAMBURG//GERMANY/; MAX DELBRUCK CENTRUM MOLEK MED/BERLIN//GERMANY/
Journal: NUCLEIC ACIDS RESEARCH, 1995, V23, N20 (OCT 25), P4023-4028
ISSN: 0305-1048
Language: ENGLISH Document Type: ARTICLE
Abstract: Alternative splicing of the p53 transcript which so far has been demonstrated only in the murine system has been proposed as a general regulatory mechanism for the generation of functionally different p53 proteins, We analyzed by RT-PCR the pattern of p53 mRNAs within the region spanning exons In and II of the p53 gene in 13 different tissues from two independent mouse strains, in 10 different rat tissues and in six different human tissues, PCR products of the expected sizes, corresponding to the normally *spliced* and the *alternatively* *spliced* *p53* mRNAs, were detected in mice, *Alternatively* *spliced* mRNA was found at similar to 25-30% the level of the normally *spliced* *p53* mRNA in most tissues analyzed. In spleen and kidney the proportion of *alternatively* *spliced* *p53* mRNA was much lower, Surprisingly, examination of *p53* mRNAs isolated from 10 different rat tissues and six human tissues within the same region of the *p53* gene showed only products of normal size, Although a potential homologous *alternative* 3' *splice* site within intron 10 of-the human *p53* gene is present in the genomic sequence of human *p53*, the expected corresponding *alternatively* *spliced* *p53* mRNA was undetectable, These findings imply that the generation of functionally different forms of *p53* by *alternative* splicing of *p53* transcripts is a species-specific event, possibly indicating species-specific mechanisms for regulating p53 activities.

4/7/27 (Item 1 from file: 351)
DIALOG(R)File 351:DERWENT WPI

010643183 WPI Acc No: 96-140137/15

XRAM Acc No: C96-044083
XRPX Acc No: N96-117371
New antibodies specific for *alternatively* *spliced* mammalian *p53* - useful in diagnosis or prognosis of cancer, and for establishing individual treatment regimes
Patent Assignee: (HEAL-) HEALTH RES INC
Author (Inventor): KULESZ-MARTIN M F
Number of Patents: 003
Number of Countries: 011
Patent Family:

CC Number	Kind	Date	Week	
CA 2150994	A	951215	9615	(Basic)
EP 709397	A1	960501	9622	
JP 8081500	A	960326	9622	

Priority Data (CC No Date): US 259612 (940614)
Applications (CC,No,Date): CA 2150994 (950605); EP 95610034 (950614); JP 95169323 (950613)
Language: English
EP and/or WO Cited Patents: 7.Jnl.Ref; EP 652232
Designated States (Regional): BE; CH; DE; DK; FR; GB; LI; NL; SE
Abstract (Basic): CA 2150994 A

A novel poly- or monoclonal antibody (Ab) to a mammalian, pref. mouse or human, p53as, esp. directed against a portion of the human wild type p53 intron 10 sequence encoding the peptide sequence SLRPFKALVREKGHRPSHSC. The p53as pref. contains a portion identical to the wild type p53 gene of the animal.

USE - The Ab is useful in diagnosis and prognosis of human cancer, and to establish treatment plans for individual patients (claimed). It can also be used (not claimed) to study p53 and p53as (or their relative expressions) and when injected into cells may cause cell cycle arrest. Vectors contg. p53as cDNA sequences may be used in similar studies and for gene therapy of cancers and other proliferative disorders such as psoriasis (p53as is a tumour suppressor).

Dwg.0/11

Derwent Class: B04; D16; S03;
Int Pat Class: A61K-039/395; C07K-016/22; C07K-016/30; C07K-016/32; C12N-015/02; C12P-021/08; G01N-033/53; G01N-033/574; G01N-033/577; C12P-021/08 C12R-001-91

9/7/1 (Item 1 from file: 5)
DIALOG(R)File 5:BIOSIS PREVIEWS(R)

12214213 BIOSIS Number: 98814213
Differential induction of *p53* and p53as DNA binding activities by DNA damage
Wu Y; *Kulesz-Martin M*
Dep. Exp. Ther., Roswell Park Cancer Inst., Buffalo, NY 14263, USA
Proceedings of the American Association for Cancer Research Annual Meeting 37 (0). 1996. 581.
Full Journal Title: 87th Annual Meeting of the American Association for Cancer Research, Washington, D.C., USA, April 20-24, 1996. Proceedings of the American Association for Cancer Research Annual Meeting
ISSN: 0197-016X
Language: ENGLISH
Print Number: Biological Abstracts/RRM Vol. 048 Iss. 006 Ref. 102682

9/7/2 (Item 2 from file: 5)

DIALOG(R)File 5:BIOSIS PREVIEWS(R)

12213842 BIOSIS Number: 98813842
In vitro transcriptional activity of tumor suppressor gene product *p53*
Kaku S; Miner Z; Pajovic S; *Kulesz-Martin M*
Dep. Experimental Therapeutics, Roswell Park Cancer Inst., Buffalo, NY 14263, USA
Proceedings of the American Association for Cancer Research Annual Meeting 37 (0). 1996. 528.
Full Journal Title: 87th Annual Meeting of the American Association for Cancer Research, Washington, D.C., USA, April 20-24, 1996. Proceedings of the American Association for Cancer Research Annual Meeting
ISSN: 0197-016X
Language: ENGLISH
Print Number: Biological Abstracts/RRM Vol. 048 Iss. 006 Ref. 102311

9/7/3 (Item 3 from file: 5)
DIALOG(R)File 5:BIOSIS PREVIEWS(R)

11104383 BIOSIS Number: 97304383
Physiological protein variant of the mouse *p53* tumor suppressor gene
Wu Y; Kim S S; *Kulesz-Martin M*
Grace Cancer Drug Cent., Dep. Exp. Therapeutics, Roswell Park Cancer Inst., Buffalo, NY 14263, USA
Proceedings of the American Association for Cancer Research Annual Meeting 35 (0). 1994. 605.
Full Journal Title: 85th Annual Meeting of the American Association for Cancer Research, San Francisco, California, USA, April 10-13, 1994. Proceedings of the American Association for Cancer Research Annual Meeting
ISSN: 0197-016X
Language: ENGLISH
Print Number: Biological Abstracts/RRM Vol. 046 Iss. 007 Ref. 109736

9/7/4 (Item 4 from file: 5)
DIALOG(R)File 5:BIOSIS PREVIEWS(R)

11095009 BIOSIS Number: 97295009
Endogenous mouse *p53* protein generated by alternative splicing
Kulesz-Martin M; Liu Y; Wu Y
Grace Cancer Drug Center, Dep. Experimental Therapeutics, Roswell Park Cancer Inst., Buffalo, NY 14263, USDA
Journal of Cellular Biochemistry Supplement 0 (18C). 1994. 170.
Full Journal Title: Keystone Symposium on Tumor Suppressor Genes, Taos, New Mexico, USA, February 13-20, 1994. Journal of Cellular Biochemistry Supplement
ISSN: 0733-1959
Language: ENGLISH
Print Number: Biological Abstracts/RRM Vol. 046 Iss. 007 Ref. 100362

9/7/5 (Item 5 from file: 5)
DIALOG(R)File 5:BIOSIS PREVIEWS(R)

10260119 BIOSIS Number: 45060119
MALIGNANT KERATINOCYTES TRANSFECTED WITH TEMPERATURE-SENSITIVE MUTANT

P53 OVEREXPRESS MUTANT AND WILD TYPE *P53*
KULESZ-MARTIN M F; LISAFELD B; KISIEL N; LEE L
ROSWELL PARK CANCER INST., BUFFALO, NY 14263, USA.
84TH ANNUAL MEETING OF THE AMERICAN ASSOCIATION FOR CANCER RESEARCH, ORLANDO, FLORIDA, USA, MAY 19-22, 1993. PROC AM ASSOC CANCER RES ANNU MEET 34 (0). 1993. 538. CODEN: PAMRE
Language: ENGLISH

9/7/6 (Item 6 from file: 5)
DIALOG(R)File 5:BIOSIS PREVIEWS(R)

9104968 BIOSIS Number: 93089968
ALTERED EXPRESSION OF WILD-TYPE *P53* TUMOR SUPPRESSOR GENE DURING MURINE EPITHELIAL CELL TRANSFORMATION
HAN K-A; *KULESZ-MARTIN M F*
DEP. EXP. THERAPEUTICS, GRACE CANCER DRUG CENT., ROSWELL PARK CANCER INST., BUFFALO, N.Y. 14263.
CANCER RES 52 (3). 1992. 749-753. CODEN: CNREA
Full Journal Title: Cancer Research
Language: ENGLISH
An epidermal cell model in which initiated, benign tumor-producing and carcinoma stages were derived from a cloned parental cell strain was used to examine *p53* expression during multistage epithelial carcinogenesis. Increased steady-state levels of *p53* RNA were detected in squamous cell carcinomas compared to papilloma and normal epidermal cells. Nontumorigenic initiated cell precursors of the carcinomas exhibited normal *p53* expression, localizing altered *p53* regulation to the malignant conversion stage. Immunoprecipitation and Western immunoblot analyses demonstrated elevated levels of *p53* protein in the moderately differentiated carcinoma compared to normal cells, and negligible levels of *p53* in the poorly differentiated carcinoma cells. Sequence analysis of *p53* complementary DNA from normal and carcinoma cells revealed no mutations in the coding or 5'- and 3'-untranslated regions, suggesting a novel mechanism of *p53* inactivation.

9/7/7 (Item 7 from file: 5)
DIALOG(R)File 5:BIOSIS PREVIEWS(R)

7894478 BIOSIS Number: 40095478
ALTERED EXPRESSION OF PUTATIVE TUMOR SUPPRESSOR GENE *P53* ASSOCIATED WITH MALIGNANT CONVERSION IN A MURINE MULTISTEP CELL TRANSFORMATION MODEL
HAN K-A; *KULESZ-MARTIN M F*
GRACE CANCER DRUG CENT., ROSWELL PARK CANCER INST., BUFFALO, N.Y. 14263.
SYMPOSIUM ON GENOMIC INSTABILITY AND CANCER HELD AT THE 20TH ANNUAL MEETING OF THE KEYSTONE SYMPOSIA ON MOLECULAR AND CELLULAR BIOLOGY, TAMARRON, COLORADO, USA, FEBRUARY 4-10, 1991. J CELL BIOCHEM SUPPL 0 (15 PART D). 1991. 125. CODEN: JCBSD
Language: ENGLISH

9/7/8 (Item 8 from file: 5)
DIALOG(R)File 5:BIOSIS PREVIEWS(R)

6785089 BIOSIS Number: 36115610
OVER-EXPRESSION OF *P53* AND VL-30 IN MOUSE EPIDERMAL CARCINOMA CELLS
HAN K-A; ROTHBERG P; *KULESZ-MARTIN M*

GRACE CANCER DRUG CENT., ROSWELL PARK MEML. INST., BUFFALO, N.Y. 14263.
MEETING ON GENETIC MECHANISMS IN CARCINOGENESIS AND TUMOR PROGRESSION HELD AT THE 18TH ANNUAL MEETING OF THE UCLA (UNIVERSITY OF CALIFORNIA-LOS ANGELES) SYMPOSIA ON MOLECULAR AND CELLULAR BIOLOGY, KEYSTONE, COLORADO, USA, JANUARY 21-28, 1989. J CELL BIOCHEM SUPPL 0 (13 PART B). 1989. 30.
CODEN: JCBSD
Language: ENGLISH

9/7/9 (Item 1 from file: 351)
DIALOG(R)File 351:DERWENT WPI

010222458 WPI Acc No: 95-123713/17
XRAM Acc No: C95-056473
Image available
Purified p53as protein and antibody - useful for studying cell growth and maturation and detecting abnormal cell growth
Patent Assignee: (HEAL-) HEALTH RES INC
Author (Inventor): *KULESZ-MARTIN M F*
Number of Patents: 003
Number of Countries: 011
Patent Family:

CC Number	Kind	Date	Week	
CA 2128833	A	950203	9517	(Basic)
EP 652232	A1	950510	9523	
JP 8099998	A	960416	9625	

Priority Data (CC No Date): US 195952 (940211); US 100496 (930802)
Applications (CC,No,Date): JP 94181558 (940802); CA 2128833 (940801); EP 94610042 (940801)
Language: English
EP and/or WO Cited Patents: 2.Jnl.Ref; EP 529160; WO 9213970
Designated States (Regional): BE; CH; DE; DK; FR; GB; LI; NL; SE
Abstract (Basic): CA 2128833 A

Purified protein, p53as, present in normal cells of a mammal and identical to *p53* of the same mammal except for the C-terminal 50 amino acids, is new. Also claimed are: (1) an antibody (Ab), specific for p53as protein; (2) a purified p53as peptide; (3) a plasmid contg. an animal p53as cDNA sequence; and (4) a viral vector contg. an animal p53as cDNA sequence.

USE - The p53as system may be useful for studying cell growth and maturation, and detecting abnormal cell growth.

Dwg.0/10

Derwent Class: B04; D16;
Int Pat Class: A61K-038/00; A61K-039/395; C07K-014/525; C07K-014/82; C07K-015/12; C07K-016/24; C07K-016/32; C12N-005/10; C12N-015/02; C12N-015/09; C12N-015/12; C12P-021/02; C12P-021/08; G01N-033/53; G01N-033/574; G01N-033/577; C12P-021/08 C12R-001-91

?◂ds

Set	Items	Description
S1	63368	P53
S2	527	S1(15N)(ALTERNATIVE?)
S3	94	S2(15N)(SPLICE?)
S4	27	RD (unique items)
S5	0	S1(15N)((LACKS OR DELETED OR MISSING OR MINUS)(15N)(NEGATIVE(2N)REGULATORY(2W)DOMAIN))
S6	167	AU="KULESZ-MARTIN M":AU="KULESZ-MARTIN MF"

S7 64 RD (unique items)
S8 58 S7 NOT S4
S9 9 S8 AND P53
?◂LOGOFF

17mar97 17:42:27 User228162 Session D306.2